ClinicalEvidence

Common cold

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ABSTRACT

INTRODUCTION: Each year, children suffer up to 5 colds and adults have two to three infections, leading to time off school or work, and considerable discomfort. Most symptoms resolve within 1 week, but coughs often persist for longer. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for common cold? We searched: Medline, Embase, The Cochrane Library, and other important databases up to January 2010 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 21 systematic reviews and RCTs that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: analgesics or anti-inflammatory drugs, antibiotics, antihistamines, decongestants for short-term and for long-term relief, decongestants plus antihistamines, echinacea, steam inhalation, vitamin C, and zinc (intranasal gel or lozenges).

QUESTIONS

INTERVENTIONS

TREATMENTS

Covered elsewhere in Clinical Evidence

Acute sinusitis

Acute bronchitis

Sore throat

To be covered in future updates

Interventions to prevent common cold

Key points

- Transmission of common cold infections is mostly through hand-to-hand contact rather than droplet spread. Several types of virus can cause symptoms of colds.

  Each year, children suffer up to 5 colds and adults have two to three infections, leading to time off school or work and considerable discomfort. Most symptoms resolve within 1 week, but coughs often persist for longer.

- Nasal and oral decongestants reduce nasal congestion over 3 to 10 hours, but we don't know how effective decongestants are for longer-term relief (>10 hours).

- Antibiotics don't reduce symptoms overall, and can cause adverse effects and increase antibiotic resistance.

  Antibiotics may improve symptoms after 5 days compared with placebo in people with nasopharyngeal culture-positive *Haemophilus influenzae*, *Moraxella catarrhalis*, or *Streptococcus pneumoniae*, but it is difficult to identify which people may have these infections.

- Vitamin C seems unlikely to reduce the duration or severity of cold symptoms compared with placebo.

  We don't know whether zinc gel or lozenges, echinacea, steam inhalation, or analgesics or anti-inflammatory drugs reduce the duration of symptoms of colds.

- Antihistamines may slightly reduce runny nose and sneezing, but their overall effect seems small. Some antihistamines may cause sedation or arrhythmias.

- We found insufficient evidence to assess whether decongestants plus antihistamines are effective in reducing cold symptoms.

DEFINITION

Common colds are defined as upper respiratory tract infections that affect the predominantly nasal part of the respiratory mucosa. Because upper respiratory tract infections can affect any part of the mucosa, it is often arbitrary whether an upper respiratory tract infection is called a "cold" or "sore throat" ("pharyngitis" or "tonsillitis"), "sinusitis", "acute otitis media", or "bronchitis" (see figure 1 in review on sore throat). Sometimes all areas (simultaneously or at different times) are affected during one illness. Symptoms include sneezing, rhinorrhoea (runny nose), headache, and general malaise. In addition to nasal symptoms, half of sufferers experience sore throat, and 40% experience cough. [1] This review does not include treatments for people with acute sinusitis (see review on acute sinusitis), acute bronchitis (see review on acute bronchitis), or sore throat (see review on sore throat). One prospective US study (1246 children enrolled at birth) found that children who had frequent colds when aged 2 or 3 years were twice as likely to experience frequent colds at year 6 compared with children who had infrequent colds at 2 or 3 years (RR 2.8, 95% CI 2.1 to 3.9). [2]

INCIDENCE/ PREVALENCE

Upper respiratory tract infections, nasal congestion, throat complaints, and cough are responsible for 11% of general practice consultations in Australia. [3] Each year, children suffer about 5 such infections and adults two to three infections. [3] [4] [5] One cross-sectional study in Norwegian children aged 4 to 5 years found that 48% experienced more than two common colds annually. [6]

AETIOLOGY/ RISK FACTORS

Transmission of common cold infection is mostly through hand-to-hand contact, with subsequent passage to the nostrils or eyes — rather than, as commonly perceived, through droplets in the air. [1] Common cold infections are mainly caused by viruses (typically rhinovirus, but also coronavirus and respiratory syncytial virus, or metapneumovirus and others). For many colds, no infecting organism can be identified.

PROGNOSIS

Common colds are usually short lived, lasting a few days, with a few lingering symptoms lasting longer, especially cough. Symptoms peak within 1 to 3 days and generally clear by 1 week, although cough often persists. [1] Although they cause no mortality or serious morbidity, common colds are responsible for considerable discomfort, lost work, and medical costs.

AIMS OF INTERVENTION

To relieve symptoms, shorten the illness, or reduce complications; to reduce infectivity to others, with minimal adverse effects from treatments.

OUTCOMES

Symptom severity: includes cure rate, time away from work or school, and symptom duration; **occurrence of complications**; **adverse effects of treatment**.

METHODS

Clinical Evidence search and appraisal January 2010. The following databases were used to identify studies for this systematic review: Medline 1966 to January 2010, Embase 1980 to January 2010, and The Cochrane Database of Systematic Reviews 2009, Issue 4 (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, and containing >20 individuals of whom >80% were followed up. We required 7 days of follow-up to include studies; however, we report outcomes within the studies at shorter timeframes than these. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the US FDA and the UK MHRA, which are added to the reviews as required. Where possible, we have excluded RCTs undertaken solely in people with experimentally induced colds, although meta-analyses in some systematic reviews do include such RCTs. We have also excluded RCTs that only assessed the outcome of bacteriological clearance. We performed a broad search for RCTs of any decongestant, analgesic, or anti-inflammatory in people with common cold, and included any RCTs of sufficient quality. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 26). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included,

in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for common cold?

OPTION ANTIHISTAMINES

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- Antihistamines may slightly reduce runny nose and sneezing, but their overall effect seems small. Some antihistamines may cause sedation or arrhythmias.

Benefits and harms

Antihistamines versus placebo:

We found two systematic reviews (search date not reported, 9 RCTs, 1757 adults; 7 RCTs in adults with naturally acquired colds, 2 RCTs in adults with experimentally induced colds; [7] and search date 2003, 32 RCTs, 8228 adults and children with naturally acquired colds, 702 with experimentally induced colds [8]) and one subsequent RCT. [9]

Symptom severity

Compared with placebo Antihistamines may be marginally more effective at reducing symptoms of runny nose and sneezing at 2 days, but we don't know whether they are more effective at reducing cough frequency or at increasing the speed of recovery (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity (global)					
[7] Systematic review	1757 adults 9 RCTs in this analysis 7 RCTs in adults with naturally acquired colds, two RCTs in adults with experimentally induced colds	**Symptoms of runny nose and sneezing , 2 days** with antihistamines (chlorphenamine or doxylamine) with placebo The review included previously unpublished individual patient data comparing antihistamines (chlorphenamine or doxylamine) versus placebo	The review reported that antihistamines reduced symptoms compared with placebo, although the effects were small (see further information on studies)		
[9] RCT **3-armed trial**	37 children aged 6 to 18 years with nocturnal cough due to upper respiratory infection The remaining arm evaluated dextromethorphan (an antitussive, single bedtime dose, based on label recommendations for age)	**Cough frequency (reduction in 7-point Likert scale, comparing 1 night without treatment to a second night with treatment)** 1.58 with diphenhydramine (single bedtime dose, based on label recommendations for age) 1.38 with placebo 25 children in this analysis (12 children in the diphenhydramine group and 13 children in the placebo group)	Significance not assessed for diphenhydramine *v* placebo The study was small and outcomes were measured in 1 night		
Cure rate					
[8] Systematic review	3492 people with colds	**Proportion recovered , 1 to 2 days** 998/1825 (55%) with antihistamines alone 892/1667 (54%) with placebo	RR 0.99 95% CI 0.93 to 1.05	⟷	Not significant
[8] Systematic review	Number of people in analysis not clear 3 RCTs in this analysis	**Proportion recovered , 3 to 5 days** with antihistamines alone with placebo	RR 1.03 95% CI 0.92 to 1.16	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[8] Systematic review	Number of people in analysis not clear 4 RCTs in this analysis	**Proportion recovered , 8 to 10 days** with antihistamines alone with placebo	RR 0.95 95% CI 0.83 to 1.09	⟷	Not significant

Complications

No data from the following reference on this outcome. [7] [8] [9]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[8] Systematic review	8930 adults and children with colds 9 RCTs in this analysis 8228 adults and children with naturally acquired colds, and 702 with experimentally induced colds	**Proportion of people reporting an adverse effect** with antihistamines alone with placebo Antihistamines were particularly associated with sedation, but also with dizziness, dry mouth, and headache	RR 1.20 95% CI 1.03 to 1.40	●○○	placebo
[8] Systematic review	People in trials evaluating non-sedating antihistamines; number of people in analysis not clear 3 RCTs in this analysis	**Proportion of people reporting an adverse effect** with non-sedating antihistamines alone with placebo	RR 1.10 95% CI 0.55 to 2.18	⟷	Not significant

No data from the following reference on this outcome. [7] [9]

Further information on studies

[7] The effects of antihistamines were small. On a severity scale ranging from 0 (no symptoms) to 3 or 4 (severe symptoms), antihistamines reduced the score from baseline by about 0.25 (95% CI 0.10 to 0.40; results presented graphically) for runny nose on days 1 and 2, 0.15 (95% CI 0 to 0.30) for sneezing on day 1, and 0.30 (95% CI 0.15 to 0.45) for sneezing on day 2.

[8] The RCTs identified by the second review assessed a wide variety of antihistamines, including cetirizine, chlorphenamine, clemastine, doxylamine succinate, loratadine, promethazine hydrochloride, and terfenadine. Decongestants used in combination with antihistamines included phenylpropanolamine and pseudoephedrine.

Comment: Some non-sedating antihistamines are associated with arrhythmias and adverse interactions with other drugs. The FDA has released a warning that respiratory depression, leading to death in some

cases, has been reported when promethazine hydrochloride was given to children aged <2 years. [10] The FDA recommends not using promethazine hydrochloride in children aged <2 years, and that parents and carers seek a doctor's advice about giving promethazine hydrochloride in any form to children aged 2 years and older.

OPTION DECONGESTANTS FOR SHORT-TERM RELIEF

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- Nasal and oral decongestants reduce nasal congestion over 3 to 10 hours, but we don't know whether they are effective in the longer term (>10 hours).
- Phenylpropanolamine has been associated with an increased risk of haemorrhagic stroke.

Benefits and harms

Decongestants for short-term relief versus placebo:

We found one systematic review (search date 2006, 6 RCTs, 642 adults with naturally acquired colds; see further information on studies) [11] and one subsequent RCT. [12] We found one further case-control study that reported on adverse effects. [13]

Symptom severity

Compared with placebo for short-term relief A single dose of a decongestant (oral norephedrine, topical oxymetazoline, oral pseudoephedrine, nasal xylometazoline) may be marginally more effective than placebo at reducing congestion at 3 to 10 hours (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Nasal congestion					
[11] Systematic review	642 adults 6 RCTs in this analysis	**Congestion (measured on a subjective scale from 0–1) , 3 to 10 hours** with single dose of decongestant (oral norephedrine, topical oxymetazoline, or oral pseudoephedrine) with placebo Absolute results not reported	WMD –0.06 95% CI –0.09 to –0.03	○○○	decongestants
[11] Systematic review	606 adults 6 RCTs in this analysis	**Objective nasal airways resistance , 3 to 10 hours** with single dose of decongestant (oral norephedrine, topical oxymetazoline, or oral pseudoephedrine) with placebo Absolute results not reported	SMD –0.24 95% CI –0.4 to –0.08	○○○	decongestants
[12] RCT	61 adults with common cold	**Median time to onset of subjective relief of nasal congestion (measured by visual analogue scale [VAS] score 0–100)** 1.7 minutes with xylometazoline nasal spray 3 times per day 1.5 minutes with placebo (saline solution) 3 times per day	Reported as no significant difference P value not reported	⟷	Not significant
[12] RCT	61 adults with common cold	**Subjective relief of nasal congestion (mean VAS score from 0–100, with 0 = nose completely clear and 100 = nose completely blocked) , over first 30 minutes after dosing (assessed every 5 minutes over 30 minute period)**	P <0.025 (P value relates to the whole 30-minute period) Congestion was also significantly lower with xylometazoline at all individual 5-minute time points over the first 30 minutes	○○○	xylometazoline

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Range 24.7 mm to 25.7 mm with xylometazoline nasal spray 3 times per day Range 35.8 mm to 36.7 mm with placebo (saline solution) 3 times per day Absolute results reported graphically			
[12] RCT	61 adults with common cold	**Subjective peak relief of nasal congestion (mean VAS score from 0–100, with 0 = nose completely clear and 100 = nose completely blocked)** 20.7 mm with xylometazoline nasal spray 3 times per day 31.5 mm with placebo (saline solution) 3 times per day	P = 0.03	○○○	xylometazoline
[12] RCT	61 adults with common cold	**Median time to subjective peak relief of nasal congestion** 30 minutes with xylometazoline nasal spray 3 times per day 30 minutes with placebo (saline solution) 3 times per day Absolute results not reported	Reported as no significant difference P value not reported	⟷	Not significant
[12] RCT	61 adults with common cold	**Total cold symptom score (individual symptoms of runny nose, blocked nose, sore throat, cough, sneezing, and ear ache, each assessed on a 4-point scale where 0 = not present, 1 = mild, 2 = moderate, and 3 = severe) , day 1 of treatment** 25.71 with xylometazoline nasal spray 3 times per day 35.79 with placebo (saline solution) 3 times per day Absolute results not reported	P = 0.022	○○○	xylometazoline

Complications

No data from the following reference on this outcome. [11] [12]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[11] Systematic review	448 adults 2 RCTs in this analysis	**Adverse effects** 25/226 (11%) with single dose of decongestant (oral norephedrine, topical oxymetazoline, or oral pseudoephedrine)	OR 1.43 95% CI 0.75 to 2.72	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		18/222 (8%) with placebo Adverse effects included insomnia, headache, and hypertension			
[12] RCT	61 adults with common cold	**Adverse effects** 7/29 (24%) with xylometazoline nasal spray 9/32 (28%) with placebo (nasal spray) 7 patients reported a total of 8 adverse effects in the xylometazoline group. 9 patients reported a total of 11 adverse effects in the placebo group The most frequently occurring adverse effects were headache and dysmenorrhoea No patients reported any symptoms suggestive of rhinitis medicamentosa	Significance not assessed		
Haemorrhagic stroke risk					
[13] Case control	2078 people 702 people with a history of haemorrhagic stroke versus 1376 people with no history of stroke	**Risk of haemorrhagic stroke** with use of cold preparations containing phenylpropanolamine with no use of cold preparations containing phenylpropanolamine	RR 1.50 95% CI 0.85 to 2.65 (phenylpropanolamine *v* no phenylpropanolamine) The study was too small to draw definitive conclusions. Formulations containing phenylpropanolamine have mostly been reformulated or withdrawn by manufacturers in the UK	⟷	Not significant

Further information on studies

[11] The review found no RCTs in children. This Cochrane review has been withdrawn as it is awaiting update. We will report the updated review in a future issue of this *Clinical Evidence* review.

Comment: We found one further systematic review (search date 2007, 7 crossover RCTs, 113 people), which found that a single dose of phenylephrine significantly reduced nasal airway resistance compared with placebo at 30 to 90 minutes. [14] However, the review did not report clinical outcomes but reported nasal airways resistance as measured by a modified Butler-Ivy airflow device, so we have not reported it further.

OPTION DECONGESTANTS FOR LONG-TERM RELIEF

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether nasal decongestants are effective in the longer term (>10 hours).

Benefits and harms

Decongestants for long-term relief versus placebo:

We found one systematic review (search date 2006, 7 RCTs, 734 adults with naturally acquired colds; see further information on studies) [11] and one subsequent RCT. [15]

Symptom severity

Compared with placebo for long-term relief We don't know whether decongestants are more effective at improving nasal congestion at up to 5 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Nasal congestion					
[11] Systematic review	443 people with naturally acquired colds 2 RCTs in this analysis	**Nasal congestion , after last treatment dose** with nasal decongestants (multiple doses) with placebo Absolute results not reported	WMD –0.03 95% CI –0.07 to 0 The review reported that the difference was of borderline significance The RCTs identified by the review did not specify method of randomisation	○○○	nasal decongestants
[11] Systematic review	432 people with naturally acquired colds 2 RCTs in this analysis	**Objective nasal airways resistance , 3 to 5 days** with nasal decongestants (multiple doses) with placebo Absolute results not reported	WMD –0.04 95% CI –0.06 to –0.01 The RCTs identified by the review did not specify method of randomisation	○○○	nasal decongestants
[15] RCT	216 people aged 18 to 65 years with common cold	**Subjective measure of nasal congestion using a 7-point categorical scale (measuring symptoms of nasal congestion, nasal runniness, sneezing) , day 1** with oral pseudoephedrine 4 times per day with placebo Absolute results not reported	Reported as no significant difference between groups P value not reported See further information on studies	⟷	Not significant
[15] RCT	216 people aged 18 to 65 years with common cold	**Subjective measure of nasal congestion using a 7-point categorical scale (measuring symptoms of nasal congestion, nasal runniness, sneezing) , day 3** with oral pseudoephedrine 4 times per day with placebo Absolute results not reported	Reported as no significant difference between groups P value not reported See further information on studies	⟷	Not significant

Complications

No data from the following reference on this outcome. [11] [15]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[15] RCT	216 people aged 18 to 65 years with common cold	**Adverse effects** with oral pseudoephedrine 4 times per day	Except for a higher incidence of insomnia with pseudoephedrine (10.2%), the RCT reported that adverse effects with pseu-		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with placebo	doephedrine were similar to those with placebo (further numerical details and statistical analysis not reported)		

No data from the following reference on this outcome. [11]

Further information on studies

[11] This Cochrane review has been withdrawn as it is awaiting update. We will report the updated review in a future issue of this *Clinical Evidence* review.

[15] The RCT also reported subjective symptom scores measured by visual analogue scale (VAS; 100-mm scale where 0 = nose completely clear and 100 = nose completely blocked). The RCT reported that "a pooled analysis of days 1 and 3 data showed a VAS score decrease of 7.0% (P = 0.072) for the 0.5- to 3-hour interval and 8.0% (P = 0.43) for the 0.5- to 4-hour interval on pseudoephedrine. Pseudoephedrine was associated with a 1.4 times (mean change from baseline pseudoephedrine, –0.43; placebo, –0.18; P = 0.059) greater reduction in mean nasal congestion using daily diary categorical scale scores when compared with placebo".

Comment: See harms on decongestants for short-term relief, p 5 .

See comment on decongestants for short-term relief, p 5 .

OPTION DECONGESTANTS PLUS ANTIHISTAMINES

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether decongestants plus antihistamines reduce cold symptoms or cold duration as we found insufficient RCT evidence.

Benefits and harms

Decongestants plus antihistamines versus placebo:

We found one systematic review (search date 2003; see further information on studies), which included RCTs that compared antihistamines in combination with decongestants with or without other agents versus placebo. [8] We have only reported on RCTs that compared the effects of decongestants plus antihistamines alone versus placebo and reported on our outcomes of interest. The review did not separately pool data on decongestants plus antihistamines alone so we have reported included RCTs separately. The review included three RCTs of sufficient quality.

Symptom severity

Compared with placebo Decongestants plus antihistamines may be more effective at improving some overall symptoms scores at up to 5 days. However, results were inconsistent between studies, and the clinical importance of some improvements is unclear (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[8] Systematic review	283 adults with common cold Data from 1 RCT	**Overall response evaluated by a physician on a 4-point scale , day 3** with loratadine plus pseu-doephedrine with placebo	P = 0.01 Results based on outcomes from 92% (261/283) of people	○○○	decongestant plus antihistamine

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute results not reported			
[8] Systematic review	283 adults with common cold Data from 1 RCT	**Overall response evaluated by a physician on a 4-point scale , day 5** with loratadine plus pseudoephedrine with placebo Absolute results not reported	P = 0.02 Results based on outcomes from 92% (261/283) of people	○○○	decongestant plus antihistamine
[8] Systematic review	283 adults with common cold Data from 1 RCT	**Mean subjective severity scores of nasal obstruction (measured on a 4-point scale) , days 1 to 5** with loratadine plus pseudoephedrine with placebo	P <0.05 The review reported that the difference in mean severity score between groups for any individual day was 0.3 severity points at most (day 1: 1.8 with loratadine plus pseudoephedrine *v* 2.1 with placebo; day 2: 1.7 with loratadine plus pseudoephedrine *v* 1.9 with placebo; day 3: 1.4 with loratadine plus pseudoephedrine *v* 1.7 with placebo; day 4: 1.3 with loratadine plus pseudoephedrine *v* 1.6 with placebo; day 5: 1.2 with loratadine plus pseudoephedrine *v* 1.5 with placebo)	○○○	decongestant plus antihistamine
[8] Systematic review	92 adults with common cold Data from 1 RCT	**Mean severity score of nasal obstruction measured on a 4-point scale (absent, mild, moderate, severe)** with dexchlorpheniramine plus pseudoephedrine with placebo Absolute results reported graphically	Reported as no significant difference P value not reported	⟷	Not significant
[8] Systematic review	86 adults with common cold Data from 1 RCT	**Mean daily subjective severity scores scored on a 5-point scale , day 2 to 5** with dexbrompheniramine maleate plus pseudoephedrine with placebo Absolute results reported graphically	P <0.05 for each individual day, days 2 to 5	○○○	decongestant plus antihistamine

Complications

No data from the following reference on this outcome. [8]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[8] Systematic review	426 people with common cold 3 RCTs in this analysis	**Dry mouth** 49/215 (23%) with decongestants plus antihistamines 24/211 (11%) with placebo	OR 4.02 95% CI 1.89 to 8.51	●●○	placebo

Further information on studies

[8] This Cochrane review has been withdrawn as it is awaiting update. We will report the updated review in a future issue of this *Clinical Evidence* review.

[8] In reviewing the evidence on decongestants plus antihistamines (including RCTs that had also included other additional treatments as part of the combination therapy), the review noted that in most trial reports there was insufficient data to judge the effect size and thus the clinical importance. The review concluded that decongestants plus antihistamines might lead to some general improvement and relief from a blocked or runny nose, although there is not enough evidence to be certain.

Comment: None.

OPTION ANALGESICS OR ANTI-INFLAMMATORY DRUGS

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether analgesics or anti-inflammatory drugs reduce the duration of symptoms of colds.

Benefits and harms

Analgesics or anti-inflammatory drugs versus placebo:

We found one systematic review (search date 2009) on non-steroidal anti-inflammatory drugs (NSAIDs). [16] The review included 6 RCTs comparing NSAIDs versus placebo and pooled data. However, three RCTs were in people with experimentally induced colds. We have not reported these RCTs further. Of the remaining three RCTs, one did not report on efficacy outcomes. We have therefore reported the two remaining RCTs separately below.

Symptom severity

Analgesics or anti-inflammatory drugs compared with placebo We don't know whether ibuprofen or loxoprofen are more effective than placebo at improving symptom scores or at reducing the duration of cold (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall symptoms					
[16] Systematic review	174 adults aged 18 to 65 years Data from 1 RCT	**Sum of overall symptom score (mean)** 76.4 with loxoprofen 75.1 with placebo	SMD +0.03 95% CI –0.27 to +0.32	⟷	Not significant
[16] Systematic review	174 adults aged 18 to 65 years Data from 1 RCT	**Mean duration of cold** 8.9 days with loxoprofen 8.4 days with placebo	Mean difference +0.55 days 95% CI –0.43 days to +1.53 days	⟷	Not significant
[16] Systematic review	174 adults aged 18 to 65 years Data from 1 RCT	**Mean restriction of daily activities** 2.1 days with loxoprofen	Mean difference –0.56 days 95% CI –1.24 days to +0.12 days	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		2.7 days with placebo			
Individual symptoms					
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Throat irritation score (mean)** 3.29 with ibuprofen 2.98 with placebo	SMD +0.13 95% CI –0.31 to +0.57 The review reported that allocation sequence and sequence generation were unclear	⟷	Not significant
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Headache score (mean)** 1.42 with ibuprofen 2.36 with placebo	SMD –0.42 95% CI –0.87 to +0.02 The review reported that allocation sequence and sequence generation were unclear	⟷	Not significant
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Score of pain in muscle/joints (mean)** 0.38 with ibuprofen 0.74 with placebo	SMD –0.27 95% CI –0.71 to +0.17 The review reported that allocation sequence and sequence generation were unclear	⟷	Not significant
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Cough score (mean)** 4.66 with ibuprofen 3.83 with placebo	SMD +0.26 95% CI –0.81 to +0.70 The review reported that allocation sequence and sequence generation were unclear	⟷	Not significant
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Sneezing score (mean)** 2.21 with ibuprofen 3.33 with placebo	SMD –0.56 95% CI –1.01 to –0.11 The review reported that allocation sequence and sequence generation were unclear	○○○	ibuprofen
[16] Systematic review	80 adults, mean age 30 years Data from 1 RCT	**Nasal obstruction score (mean)** 5.71 with ibuprofen 5.6 with placebo	SMD +0.05 95% CI –0.39 to +0.49 The review reported that allocation sequence and sequence generation were unclear	⟷	Not significant

Complications

No data from the following reference on this outcome. [16]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[16] Systematic review	174 adults aged 18 to 65 years Data from 1 RCT	**Overall adverse effects** 8/84 (10%) with loxoprofen 1/90 (1%) with placebo	RR 8.57 95% CI 1.10 to 67.0 Further details not reported	●●●	placebo

Further information on studies

Comment: None.

OPTION ECHINACEA

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether echinacea is more effective than placebo at reducing the severity or duration of cold symptoms.

Benefits and harms

Echinacea versus placebo:

We found two systematic reviews (search dates 2007 [17] and 2006 [18]). The reviews had different inclusion criteria, performed a different analysis, and came to differing conclusions. The first review excluded combinations of echinacea with other herbs, included RCTs that reported on severity of symptoms or duration, and did not pool data because of clinical heterogeneity between included RCTs (preparation used, trial design, and outcomes reported). It included 14 RCTs on treatment. [17] The second review [18] included RCTs in which echinacea had been used with or without a supplement, all of which reported on cold duration. In the analysis of effects on cold duration, it included 4 RCTs that were included in the first review, two RCTs that were excluded by the first review because of methods used, and included one RCT not included in the first review. The second review pooled data and came to slightly different conclusions to the first review (see further information on studies).

Symptom severity

Compared with placebo We don't know whether echinacea is more effective at reducing cold symptoms or at reducing the duration of cold (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity (global)					
[17] Systematic review	1078 people with a cold 7 RCTs in this analysis	**Overall symptom score , 2 to 4 days** with echinacea with placebo	2 RCTs found that echinacea significantly reduced overall symptom score compared with placebo 5 RCTs found no significant difference between groups The review did not pool data, see further information on studies		
[17] Systematic review	1295 people with a cold 10 RCTs in this analysis	**Overall symptom score , 5 to 10 days** with echinacea with placebo	5 RCTs found that echinacea significantly reduced overall symptom score compared with placebo 5 RCTs found no significant difference between groups The review did not pool data, see further information on studies		
Nasal symptoms					
[17] Systematic review	890 people with a cold 6 RCTs in this analysis	**Nasal symptoms , 2 to 4 days** with echinacea with placebo	2 RCTs found that echinacea significantly reduced nasal symptoms compared with placebo 4 RCTs found no significant difference between groups		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
			The review did not pool data, see further information on studies		
[17] Systematic review	1270 people with a cold 10 RCTs in this analysis	**Nasal symptoms , 5 to 10 days** with echinacea with placebo	Three RCTs found that echinacea significantly reduced nasal symptoms compared with placebo 7 RCTs found no significant difference between groups The review did not pool data, see further information on studies		
Symptom duration					
[17] Systematic review	160 people Data from 1 RCT	**Mean symptom duration** 9.30 days with echinacea 12.90 days with placebo	SMD –1.83 95% CI –2.20 to –1.46	○○○	echinacea
[17] Systematic review	142 people Data from 1 RCT	**Mean symptom duration** 6.27 days with echinacea 5.75 days with placebo	SMD +0.22 95% CI –0.11 to +0.55	⟷	Not significant
[18] Systematic review	1630 people with a cold 7 RCTs in this analysis	**Reduction in duration of cold** with echinacea with placebo Absolute results reported graphically	WMD –1.44 days 95% CI –2.24 days to –0.64 days P = 0.01 There was significant heterogeneity among RCTs (see further information on studies) Some echinacea preparations contained other supplements and some did not	○○○	echinacea
Combined measure of severity and duration of cold					
[17] Systematic review	1103 people with a cold 6 RCTs in this analysis	**Combined measure of severity and duration of cold** with echinacea with placebo	1 RCT found that echinacea was significantly more effective than placebo The remaining 5 RCTs found no significant difference between echinacea and placebo The review did not pool data, see further information on studies		

Complications

No data from the following reference on this outcome. [17] [18]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[17] Systematic review	1691 people with a cold	**Proportion of people reporting adverse effects** 207/804 (26%) with echinacea	None of the individual RCTs reporting on adverse effects found any significant difference between echinacea and placebo		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	11 RCTs in this analysis	187/887 (21%) with placebo	Results not pooled owing to heterogeneity		
Withdrawals caused by adverse effects					
[17] Systematic review	80 people with a cold Data from 1 RCT	**Withdrawals caused by adverse effects** 1/41 (2%) with echinacea 0/39 (0%) with placebo	OR 2.93 95% CI 0.12 to 74.0	⟷	Not significant
[17] Systematic review	436 people with a cold Data from 1 RCT	**Withdrawals caused by adverse effects** 6/215 (3%) with echinacea 1/221 (0.5%) with placebo	RR 6.32 95% CI 0.75 to 52.91	⟷	Not significant
Rash					
[17] Systematic review	Children with a cold Data from 1 RCT	**Proportion of children with rash** 7% with echinacea 3% with placebo Absolute numbers not reported	P = 0.008	○○○	placebo

No data from the following reference on this outcome. [18]

Further information on studies

[17] [18] The second review, which pooled data, also performed a sensitivity analysis of RCTs in which no supplement had been given with echinacea. [18] It found no significant difference between groups in cold duration (3 RCTs, 915 people; WMD –1.57 days, 95% CI –4.34 days to +1.19 days, P = 0.27). The authors of the first review [17] noted that the second review [18] had come to more favourable conclusions on the effects of echinacea than it had. The authors of the first review noted that the second review had included trials on highly variable echinacea products and pooled data, whereas they had chosen not to because of the clinical heterogeneity between trials. [17]

Comment: Echinacea is not a single product. There are >200 different preparations based on different plants, different parts of the plant (roots, herbs, whole plant), and different methods of extraction. The weakness of trial methods and differences in interventions make it difficult to draw conclusions about effectiveness. Large RCTs may be difficult because echinacea is not patentable, and each producer controls a small share of the market. The authors of the first systematic review [17] received personal information about several unpublished studies that they were not able to include.

Isolated cases of anaphylaxis have been reported in people taking echinacea. [19] [20]

OPTION STEAM INHALATION

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether steam inhalation reduces the duration of symptoms of colds.

Benefits and harms

Steam inhalation versus sham inhalation:

We found one systematic review (search date 2005), which compared steam inhalation at 40 °C to 47 °C versus sham inhalation (air at 30 °C or higher). [21] The review (6 RCTs, 319 people; 4 RCTs in people with naturally acquired

colds, 2 in people with experimentally induced colds) could not perform a meta-analysis of all the RCTs because of heterogeneity in populations and methods used to assess symptoms, and poor reporting in some of the RCTs. We have reported the results from the meta-analysis, which pooled data from two RCTs in people with naturally acquired colds.

Symptom severity

Compared with sham inhalation We don't know whether steam inhalation is more effective than sham inhalation (air at 30 °C or higher) at reducing the proportion of people with symptoms of common cold immediately after treatment or at 4 days, as we found insufficient evidence from weak studies (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom relief					
[21] Systematic review	146 people with naturally acquired colds 2 RCTs in this analysis	**Proportion of people with symptoms , immediately after treatment or at 4 days** 29/77 (38%) with steam inhalation at 40 °C to 47 °C 46/69 (67%) with sham inhalation (air at 30 °C or higher) It is unclear whether sham inhalation is a valid control	RR 0.56 95% CI 0.40 to 0.79 The review stated that the RCTs used different symptom score indices, but did not specify which indices were used	●○○	steam inhalation

Complications

No data from the following reference on this outcome. [21]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[21] Systematic review	People with naturally acquired or experimentally induced colds	**Adverse effects** with steam inhalation at 40 °C to 47 °C with sham inhalation (air at 30 °C or higher) The RCTs identified by the review found no evidence of adverse effects There may be a danger from spilling hot water and from nosocomial infections related to humidifier units			

Further information on studies

Comment: None.

OPTION ZINC

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- We don't know whether zinc gel or lozenges reduce the duration of symptoms of colds.

Benefits and harms

Zinc lozenges versus placebo:

We found three systematic reviews (search dates 1997, [22] 1998, [23] and 2003 [24]), which compared zinc lozenges (gluconate or acetate) versus placebo for the treatment of naturally acquired colds. The reviews had different inclusion and exclusion criteria. The first and second reviews performed a meta-analysis, [22] [23] whereas the third review was narrative in character, [24] and did not perform a meta-analysis. The third review [24] identified 10 RCTs that were included in the two other reviews [22] [23] (including all the RCTs identified by both earlier reviews and 1 RCT excluded by the first review owing to poor methods, and 2 RCTs excluded by the second review because they involved people with experimentally induced colds). In addition, the third review identified two RCTs carried out subsequent to the earlier reviews, the results from which we report separately. [24] We found one subsequent RCT. [25] We found one further systematic review, which did not report numerical results of statistical analyses, so we have not reported it further here (see comments). [26] One review identified case reports on adverse effects associated with zinc preparations (see further information on studies). [27]

Symptom severity

Zinc lozenges compared with placebo We don't know whether zinc lozenges are more effective at reducing symptom duration (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom duration					
[22] Systematic review	754 people with colds 7 RCTs in this analysis 681 people (5 RCTs) with naturally acquired colds, 73 people (2 RCTs) with experimentally induced colds	**Continuing symptoms , 7 days** 14/93 (15%) with zinc lozenges 46/94 (49%) with placebo	RR 0.31 95% CI 0.18 to 0.52 Random effects model	●●○	zinc lozenges
[23] Systematic review	People with naturally acquired colds	**Continuing symptoms , 7 days** with zinc lozenges with placebo Absolute results reported graphically	OR 0.52 95% CI 0.25 to 1.20 The review found statistical heterogeneity (see further information on studies)	⟷	Not significant
[24] Systematic review	48 people with naturally acquired colds Data from 1 RCT	**Mean duration of symptoms** 4.5 days with zinc lozenges 8.1 days with placebo	P <0.01	○○○	zinc lozenges
[24] Systematic review	281 people with naturally acquired colds Data from 1 RCT	**Mean duration of symptoms** 7 days with zinc lozenges 7 days with placebo	P = 0.45	⟷	Not significant
[25] RCT	129 children with common cold symptoms (median age 5.2 years)	**Median time to resolution of all cold symptoms** 6 days with zinc syrup 6 days with placebo syrup	P = 0.09	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[25] RCT	129 children with common cold symptoms (median age 5.2 years)	**Median time to resolution of nasal symptoms** 5 days with zinc syrup 5 days with placebo syrup	P = 0.20	⟷	Not significant
Symptom severity score					
[25] RCT	129 children with symptoms of common cold (median age 5.2 years)	**Total symptom severity score , day 2 of treatment** 3.6 with zinc syrup 4.9 with placebo syrup	Reported as P = 0.000	○○○	zinc
[25] RCT	129 children with symptoms of common cold (median age 5.2 years)	**Total symptom severity score , day 3 of treatment** 2.0 with zinc syrup 2.8 with placebo syrup	P = 0.007	○○○	zinc
[25] RCT	129 children with symptoms of common cold (median age 5.2 years)	**Total symptom severity score , day 4 of treatment** 0.8 with zinc syrup 1.2 with placebo syrup	P = 0.041	○○○	zinc
[25] RCT	129 children with symptoms of common cold (median age 5.2 years)	**Total symptom severity score , day 5 of treatment** 0.3 with zinc syrup 0.7 with placebo syrup	P = 0.048	○○○	zinc

Complications

No data from the following reference on this outcome. [22] [23] [24] [25]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[22] Systematic review	754 people with colds 7 RCTs in this analysis 681 people with naturally acquired colds, 73 people with experimentally induced colds	**Adverse effects , 7 days** with zinc lozenges with placebo In some of the RCTs, a higher proportion of people had nausea, altered taste, dry mouth, abdominal pain, and headache with zinc lozenges compared with placebo, but the review did not state whether the difference was significant			
[25] RCT	129 children with symptoms of common cold (mean age 5.2 years) Data from 1 RCT	**Adverse effects** 25% with zinc 27% with placebo Absolute results not reported The most commonly reported adverse effect was bad taste, but	Reported as no significant difference P value not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		several other minor adverse effects were also reported. None were significantly different between the zinc group and the placebo group			

No data from the following reference on this outcome. [23]

Intranasal zinc gel versus placebo:

We found one systematic review (search date 2007), [28] which included three RCTs [29] [30] [31] and pooled data. Two of the included RCTs used a high dose of zinc (daily dose 2.1 mg), whereas the third RCT used a lower dose (daily dose 0.044 mg). One review identified case reports on adverse effects associated with zinc preparations (see further information on studies). [27]

Symptom severity

Zinc intranasal gel compared with placebo We don't know whether intranasal zinc is more effective at reducing the proportion of people with symptoms at 3 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom duration					
[28] Systematic review	451 adults with common cold 3 RCTs in this analysis	**Any symptoms persisting on day 3** 137/229 (60%) with zinc 212/222 (95%) with placebo	RR 0.62 95% CI 0.18 to 2.19 using a random effects analysis Result found to be significant with fixed effects analysis; see further information on studies Significant heterogeneity among RCTs. Caution is required in interpreting results	⟷	Not significant

Complications

No data from the following reference on this outcome. [28]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Overall adverse effects					
[28] Systematic review	78 people with common cold Data from 1 RCT	**Adverse effects** 9/40 (23%) with zinc 3/38 (8%) with placebo	Significance not reported		
Nasal stinging or burning					
[28] Systematic review	78 people with common cold Data from 1 RCT	**Stinging or burning sensation** 5/40 (13%) with intranasal zinc (daily dose 2.1 mg)	Significance not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		2/38 (5%) with placebo			

Further information on studies

[23] **Zinc lozenges versus placebo** The results were statistically heterogeneous, which may be because the RCTs in the reviews used different zinc formulations, were undertaken in people with different types of virus, or because of unknown factors.

[28] **Intranasal zinc versus placebo: fixed effects analysis:** The review found a significant difference between groups using a fixed effects analysis (3 RCTs, 451 people; RR 0.63, 95% CI 0.56 to 0.70). However, there was a large degree of heterogeneity among RCTs (P value not reported; I^2 = 99.2%). With regard to the high degree of heterogeneity, one RCT using a high dose of intranasal zinc found a large treatment effect at 3 days (213 people; RR 0.32, 95% CI 0.24 to 0.42), whereas another high-dose RCT found a borderline effect (78 people; RR 0.78, 95% CI 0.61 to 1.00) and a third RCT using a lower dose of zinc found less effect (160 people; RR 0.96, 95% CI 0.91 to 1.02). **Heterogeneity:** The review reports that heterogeneity was caused in large part by the study with the large treatment effect. In addition, two RCTs only included people with symptoms for <24 hours, whereas the other RCT only included people with symptoms for 24–48 hours). The review also identified 10 case reports of permanent anosmia (see below). [28]

[28] **Harms with intranasal zinc** One report identified a series of 10 case reports of permanent anosmia (loss of smell) associated with intranasal zinc gluconate. [28] The 10 people (aged 31–55 years) had immediate severe burning of the nose followed by severe hyposmia with parosmia or anosmia. The people had previously reported normal taste and smell and had no other causative history to account for the loss.

Comment: We found one further systematic review, which examined the effects of zinc lozenges, nasal sprays, or gels versus placebo. [26] It did not report numerical results or statistical analysis. It included 14 RCTs, which were evaluated against 11 previously determined quality criteria (including validated case definition, double blinding, sample size calculation, etc.). In total, 4 RCTs fulfilled all the 11 quality criteria. Of these, one RCT found a positive effect with zinc nasal gel, while three RCTs found no effect with zinc lozenges or nasal spray. It concluded that the therapeutic effects of zinc lozenges have yet to be demonstrated.

The Cochrane review comparing zinc lozenges versus placebo has been withdrawn as it is awaiting update. [22]

OPTION VITAMIN C

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- Vitamin C seems unlikely to reduce the duration or severity of cold symptoms compared with placebo.

Benefits and harms

Vitamin C versus placebo:

We found one systematic review (search date 2006). [32] The review included RCTs of cold prophylaxis and treatment. We have only included data on treatment. The review included any RCTs using vitamin C (200 mg or more daily) compared with placebo in people with the common cold.

Symptom severity

Compared with placebo Vitamin C may be no more effective at reducing symptom severity or mean duration of symptoms (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[32] Systematic review	2753 cold episodes in adults 4 RCTs in this analysis The review included data from 8 different trial arms	**Symptom severity (measured by mean days indoors or off work or by mean symptom severity score)** with vitamin C (commenced after cold symptoms had begun) with placebo Absolute results reported graphically The RCTs included in the analysis used a variety of therapeutic protocols (see further information on studies for full details)	SMD –0.07 95% CI –0.16 to +0.02	⟷	Not significant
Symptom duration					
[32] Systematic review	3294 cold episodes in adults 7 RCTs in this analysis The review included data from 11 different trial arms	**Mean duration of symptoms per episode** with vitamin C (commenced after cold symptoms had begun) with placebo Absolute results reported graphically The RCTs included in the analysis used a variety of therapeutic protocols (see further information on studies for full details)	WMD –2.54 days 95% CI –10.09 days to +5.02 days	⟷	Not significant

Complications

No data from the following reference on this outcome. [32]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[32] Systematic review	People with common cold	**Adverse effects** with vitamin C (commenced after cold symptoms had begun) with placebo The review did not report on adverse effects for RCTs using vitamin C as treatment, but did include data from RCTs using vitamin C as prophylaxis (see further information on studies for full details)			

Further information on studies

[32] The RCTs included in the analysis used a variety of therapeutic protocols, ranging from a single dose at the onset of cold symptoms to continued treatment for 4 days using differing regimens. The review noted that RCTs in which vitamin C was used as treatment in doses up to 4 g daily did not demonstrate any benefit, but one large RCT reported an "equivocal" benefit from the use of a very high 8-g therapeutic dose at the onset of symptoms. However, there were methodological issues in this large RCT in that one of the two placebo groups had substantial baseline differences with the vitamin C groups, and that comparisons were restricted to the placebo group that had similar baseline data to the other vitamin C arms. **Adverse effects** Seven RCTs included in the review provided data on adverse effects. In these RCTs, 2490 people took >1 g daily of vitamin C during prophylaxis compared with 2066 people taking placebo. The review stated that no serious symptoms were reported. It found that 5.8% of people taking vitamin C reported symptoms that they attributed to the medication, compared with 6.0% taking placebo (no further details reported).

Comment: None.

OPTION ANTIBIOTICS

- For GRADE evaluation of interventions for Common cold, see table, p 26 .
- Antibiotics don't reduce symptoms overall, and can cause adverse effects and increase antibiotic resistance.
- Antibiotics may improve symptoms after 5 days compared with placebo in people with nasopharyngeal culture-positive Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae, but it is difficult to identify which people may have these infections.

Benefits and harms

Antibiotics versus placebo:

We found three systematic reviews (search dates 2005, 6 RCTs; [33] not reported, 12 RCTs; [34] and 2005, 6 RCTs [35]). The systematic reviews identified several RCTs in common. The second review included 4 RCTs identified by the first review and 8 RCTs excluded from the first review owing to poor methods. [34] The third review identified 5 RCTs that were also included in one or both of the earlier reviews. [35]

Symptom severity

Compared with placebo Antibiotics may be no more effective at increasing cure rate or general improvement at 5 to 7 days in people with colds. Antibiotics may be more effective at increasing the proportion of people with clearance of purulent rhinitis at 5 to 8 days in people with acute purulent rhinitis associated with an upper respiratory tract infection (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement or cure					
[33] Systematic review	1147 people 6 RCTs in this analysis	**General improvement or cure , 7 days** 168/664 (25%) with antibiotics 170/483 (35%) with placebo	RR 0.89 95% CI 0.77 to 1.04	⟷	Not significant
[34] Systematic review	1482 children with naturally acquired colds who had symptoms in the previous 2 weeks 6 RCTs in this analysis Of the 12 RCTs identified by the review, only 6 had adequate data for analysis	**Proportion of children with worse or unchanged clinical outcome , 6 to 14 days** 309/835 (37%) with antibiotics 280/647 (43%) with placebo	RR 1.01 95% CI 0.90 to 1.13 The RR reported by the review for this outcome does not match the absolute results reported (see further information on studies for full details)	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[36] RCT	314 adults with naturally acquired colds for 1 to 30 days; <7 days in 85% of people In review [33] Full trial evaluated	**Cure rates , 5 days** with amoxicillin–clavulanic acid (co-amoxiclav) 375 mg three times daily with placebo	Reported as not significant P value not reported	⟷	Not significant
[36] RCT	61 people (20%) found to have positive nasopharyngeal cultures for *H influenzae*, *M catarrhalis*, or *S pneumoniae* In review [33] Subgroup analysis	**Cure rates , 5 days** 27% with amoxicillin–clavulanic acid (co-amoxiclav) 375 mg, three times daily 4% with placebo	P = 0.001 See comment in further information on studies	○○○	co-amoxiclav
[35] Systematic review	618 people with acute purulent rhinitis associated with an upper respiratory tract infection 4 RCTs in this analysis One RCT was excluded from the analysis as the antibiotic was topical and the placebo was a locally active agent A second RCT was excluded as it was not clear whether the rhinitis was purulent or clear	**Proportion of people with clearance of purulent rhinitis , 5 to 8 days** 254/355 (72%) with antibiotics 154/263 (59%) with placebo	RR 1.18 95% CI 1.05 to 1.33	●○○	antibiotics

Complications

No data from the following reference on this outcome. [33] [34] [35]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[33] [34] Systematic review	At least 1482 people 4 RCTs in this analysis	**Adverse effects** with antibiotics with placebo Both reviews found that adverse effects such as nausea, vomiting, headache, rash, or vaginitis occurred more often with antibiotics than with placebo			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[35] Systematic review	618 people with acute purulent rhinitis associated with an upper respiratory tract infection 4 RCTs in this analysis One RCT was excluded from the analysis as the antibiotic was topical and the placebo was a locally active agent A second RCT was excluded as it was not clear whether the rhinitis was purulent or clear	**Proportion of people with adverse effects** with antibiotics with placebo Absolute results not reported Reported adverse effects were mainly gastrointestinal, along with a small number of rashes	RR 1.46 95% CI 1.10 to 1.94	●○○	placebo

Further information on studies

[33] The relative risk (RR 1.01, 95% CI 0.90 to 1.13) surrounding clinical outcome reported by the second review does not match the absolute results reported; we have quoted it directly from the paper.

[35] If people infected with *H influenzae*, *M catarrhalis*, or *S pneumoniae* could be identified at first consultation, then treating 4 of these people with antibiotic rather than placebo would result in an average of one more recovery at 5 days (NNT 4, CI not reported). However, there is currently no means of easily identifying people with these infections at first consultation.

Comment: We found no evidence of the size of the risk of antibiotic resistance or pseudomembranous colitis.

Clinical guide:
Because most common colds are viral, the potential benefit from antibiotics is limited. Until rapid identification of those people likely to benefit is possible, the modest effects seen in trials must be weighed against the adverse effects of antibiotics, costs, and potential for inducing antibiotic resistance.

GLOSSARY

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Analgesic or anti-inflammatory drugs One systematic review added. [16] Categorisation unchanged (Unknown effectiveness) as there remains insufficient data to assess this intervention.

Decongestants for long-term relief One RCT added. [15] Categorisation of decongestants for long-term relief unchanged (Unknown effectiveness).

Decongestants for short-term relief One systematic review [11] and one RCT added. [12] Categorisation of decongestants for short-term relief unchanged (Likely to be beneficial).

Decongestants plus antihistamines One systematic review added. [8] Categorisation unchanged (Unknown effectiveness) as there remains insufficient data to assess this intervention.

Echinacea One already reported systematic review updated [17] and one further systematic review added. [18] Categorisation unchanged (Unknown effectiveness) as there remains insufficient data to assess this intervention.

Vitamin C One already reported systematic review updated. [32] Categorisation unchanged (Unlikely to be beneficial).

Zinc Two systematic reviews, [26] [28] one subsequent RCT, [25] and one report on harms [28] added. Categorisation unchanged (Unknown effectiveness) as there remains insufficient data to assess this intervention.

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GRADE **Evaluation of interventions for Common cold.**

Important outcomes			Complications, Symptom severity						
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatments for common cold?									
at least 10 (at least 3592) [7] [8] [9]	Symptom severity	Antihistamines versus placebo	4	–1	0	–2	0	Very low	Quality point deducted for incomplete reporting of results. Directness points deducted for inclusion of experimentally induced colds and for unclear clinical importance of results
7 (703) [11] [12]	Symptom severity	Decongestants for short-term relief versus placebo	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for unclear clinical importance of results
at least 3 (at least 659) [11] [15]	Symptom severity	Decongestants for long-term relief versus placebo	4	–2	0	0	0	Low	Quality points deducted for incomplete reporting of results and weak methods (randomisation not reported)
3 (461) [8]	Symptom severity	Decongestants plus antihistamines versus placebo	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for unclear clinical importance of results
2 (254) [16]	Symptom severity	Analgesics or anti-inflammatory drugs versus placebo	4	–1	0	–1	0	Low	Quality point deducted for weak methods in 1 RCT. Directness point deducted for small number of analgesics assessed
at least 10 (at least 1630) [17] [18]	Symptom severity	Echinacea versus placebo	4	–1	0	–2	0	Very low	Quality point deducted for incomplete recording of results. Directness points deducted for clinical heterogeneity between RCTs (including statistical heterogeneity in 1 analysis), significance of results depending on the analysis undertaken, and for the use of additional supplements in some RCTs
2 (146) [21]	Symptom severity	Steam inhalation versus sham inhalation	4	−3	0	0	0	Very low	Quality points deducted for sparse data, uncertainty about the validity of control, and unclear symptom score indices
10 (at least 1212) [22] [23] [24] [25]	Symptom severity	Zinc lozenges versus placebo	4	–1	–1	0	0	Low	Quality point deducted for inclusion of people with experimentally induced colds. Consistency point deducted for heterogeneity between RCTs
3 (451) [28]	Symptom severity	Intranasal zinc gel versus placebo	4	0	0	–2	0	Low	Directness points deducted for wide range of doses used in RCTs, inclusions of slightly different population, and varying significance of results depending on analysis undertaken
at least 7 (at least 3294 cold episodes) [32]	Symptom severity	Vitamin C versus placebo	4	–1	0	–1	0	Low	Quality point deducted for analysis by cold episodes not people. Directness point deducted for wide range of treatment protocols in RCTs
at least 6 (at least 1482) [33] [34] [35] [36]	Symptom severity	Antibiotics versus placebo	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results (and unclear in 1 review). Directness point deducted for inclusion of people with additional bacterial infection

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.

Common cold